**Exam 3 Test Prep**

**Substitution and Elimination**

Breaking down each reaction:

## Sn2

substitution nucleophilic bi molecular
concerted
strong nuc⁻

## E2

Elimination bi molecular
concerted
strong base

## Sn1

substitution nucleophilic uni molecular
step-wise
weak nuc⁻

## E1

Elimination uni molecular
step-wise
weak base

What is said to be the rate-determining step in an Sn1 or E1 reaction? (Circle the 2 answers)

A. Loss of a leaving group
B. Backside attack
C. Carbocation rearrangement
D. Formation of a carbocation
E. Mixing the solution of chemicals

T/F: Rate-determining steps are typically very quick

False, they are the "slow-step"

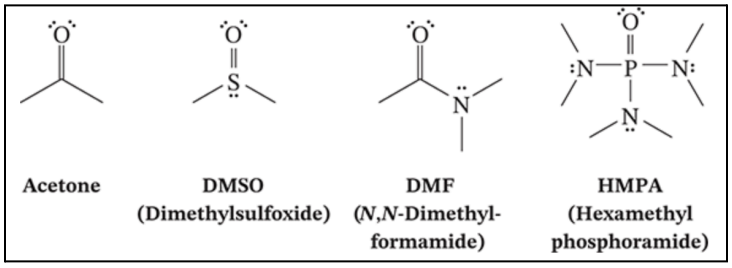
**Solvents**

Generally, polar aprotic goes with E2/SN2 and polar protic goes with SN1/E1

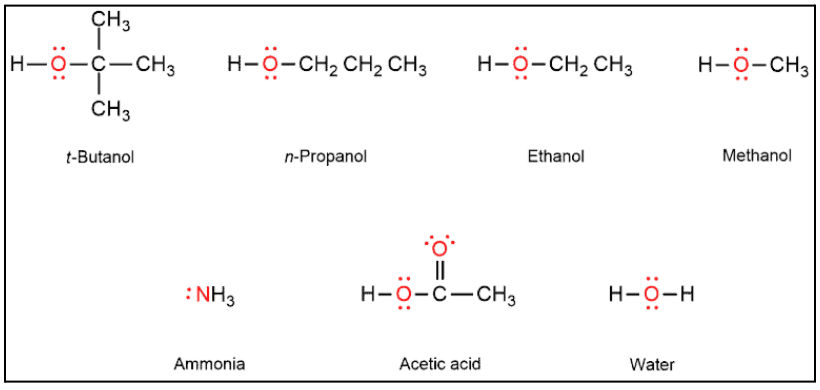
On of the major exceptions is alkoxide with like alcohol

Ex: NaOEt / EtOH

Polar Aprotic Solvents




Polar Protic Solvents



**Determining Nucleophilicity**

Charge: more negative charge, better nucelophile

Sterics: smaller the nulceophile the better it is

typically used for halogens only

Electronegativity: In polar protic solvents, EN and nulceophilicity are inverse

Polarizability: The ability of a very large atom to donate e⁻ density, regardless of solvation

Is -SH or -OH a better nulceophile?

**Determining Bascity**

Acid-base principle: Look at the conj. acid

Nulceophilicity parallels with basicity for compounds with the same element

nucleophilicity
basicity

$$RO^- > HO^- \gg RCO_2^- > ROH > H_2O$$

Nulceophilicity is not parallel to basicity for compounds with different elements

nucleophilicity

$$HS^- > N{\equiv}C^- > I^- > HO^-$$

Basicity

Identify the better nucleophile:

a. NaSH vs. H2S

actually ⊖

c. $CH_3O^-$ (In methanol) vs $CH_3O^-$ (in DMSO)

not solvated

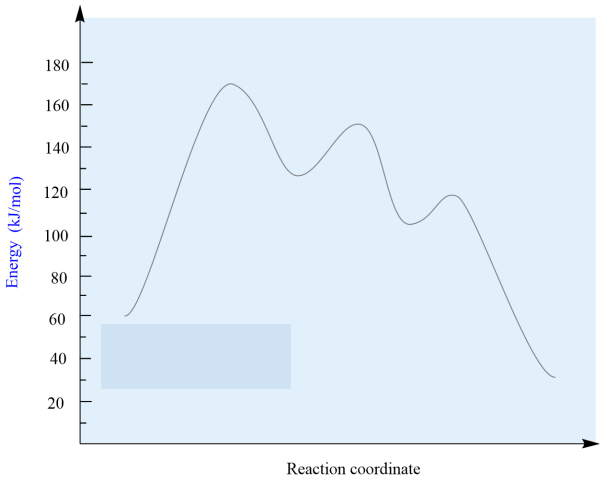
d. Ethoxide $CH_3CH_2O^-$ vs. tert-butoxide $(CH_3)_3O^-$

less sterically hindered

e. HO- vs. Cl-

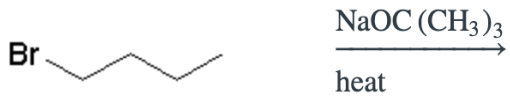
**E & S Practice**

What is true about the free energy diagram below?

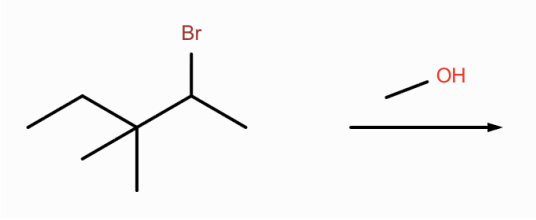


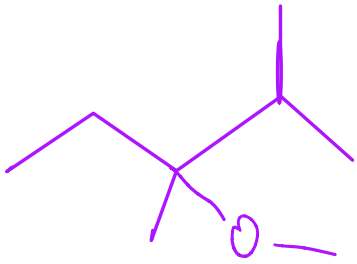

A. The reaction is an endergonic reaction, meaning Gibbs free energy is less than 0
B. The reaction is most likely an Sn2 reaction, which is unimolecular and exergonic
C. The reaction is a competing reaction between E2 and Sn2, both are endergonic, where Gibbs free energy is greater than 0
D. The reaction is most likely Sn1, which is exergonic, where Gibbs free energy is less than 0
E. The reaction is E1, an exergonic reaction, meaning Gibbs free energy is greater than 0

Give the major product and identify the reaction below:



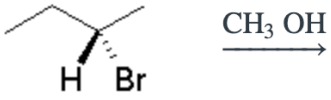

E2

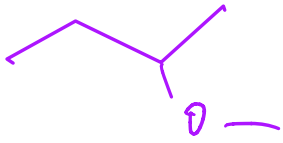


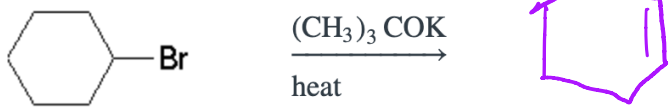
SN1

w/ methyl shift

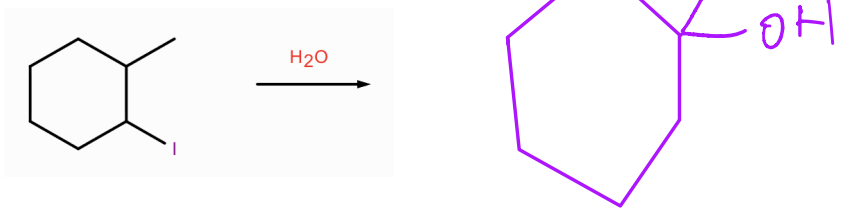


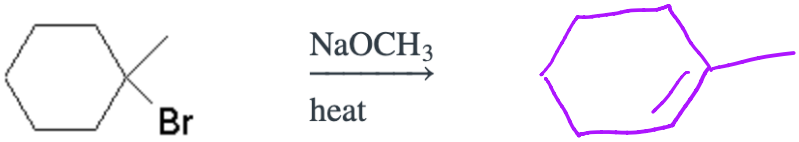
SN1 (can still happen 2° - although uncommon)




E2




SN1
w/ hydride
shift

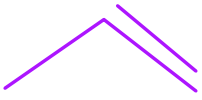



E2


SN2

or

E2



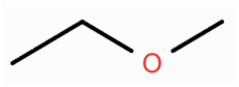
**Reaction Scenarios**

1. Emily wants to make an ether compound using 1-bromo-1-methylcyclopentane. What kind of reagents would be good for this?


   From the previous problem above, Emily mixes the reagents and heats them up in an Erlenmeyer flask. When she is determining her final product, she notices she isn't getting the desired product. How can she change her reaction conditions to get the product she wants?

- lower the temp to room temp or cooler
- favor SN1

2. Harvey is working on synthesizing a new drug. One of his reactions is taking chloroethane, sodium methoxide, and turning it into the compound below




   Unfortunately, he is completely out of his stash of aprotic solvents. Can Harvey still complete his reaction? If so, how can he do it?

yes, use the alkoxide like-alcohol

**E&S Charts**

| | Regiochemistry | Stereochemistry |
|---|---|---|
| **Sn2** | nuc$^{\ominus}$ attacks $\alpha$ carbon | Inversion of configuration |
| **E2** | Zaitsev prod is major unless using a sterically hindered (bulky) base | -stereoselective: trans major prod.<br>-stereospecific: only if there's 1 $\beta$ hydrogen |
| **Sn1** | nuc$^{\ominus}$ attacks carbocation | Racemic mixture |
| **E1** | Zaitsev is always major product | -stereoselective: trans-favored prod. |

| Strong base<br>Weak nucleophile | Strong base<br>Strong nucleophile | Weak base<br>Strong nucleophile | Weak base<br>Weak nucleophile |
|---|---|---|---|
| DBN DBU | $HO^-$ $MeO^-$ $EtO^-$ | $I^-$ $Br^-$ $Cl^-$<br>$RS^-$ $HS^-$ RSH $H_2S$ | $H_2O$ MeOH EtOH |

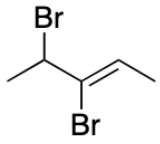
| | Strong base<br>Weak nucleophile | Strong base<br>Strong nucleophile | Weak base<br>Strong nucleophile | Weak base<br>Weak nucleophile |
|---|---|---|---|---|
| 1° | E2 | E2 $S_N2$ | $S_N2$ | |
| 2° | E2 | E2 $S_N2$ | $S_N2$ | |
| 3° | E2 | E2 | $S_N1$ | $S_N1$ E1 |

**Alkenes**

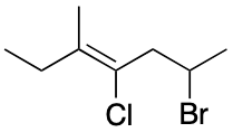
(E): priority groups are on opposite sides

(Z): priority groups are on the same side

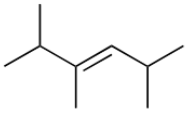
Designate E or Z for the compounds below:




Z

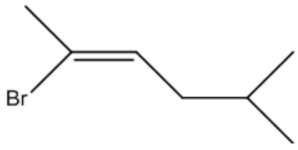



Z

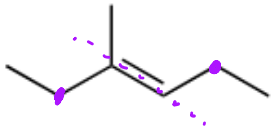


E

Name the compounds with E and Z configuration in mind:

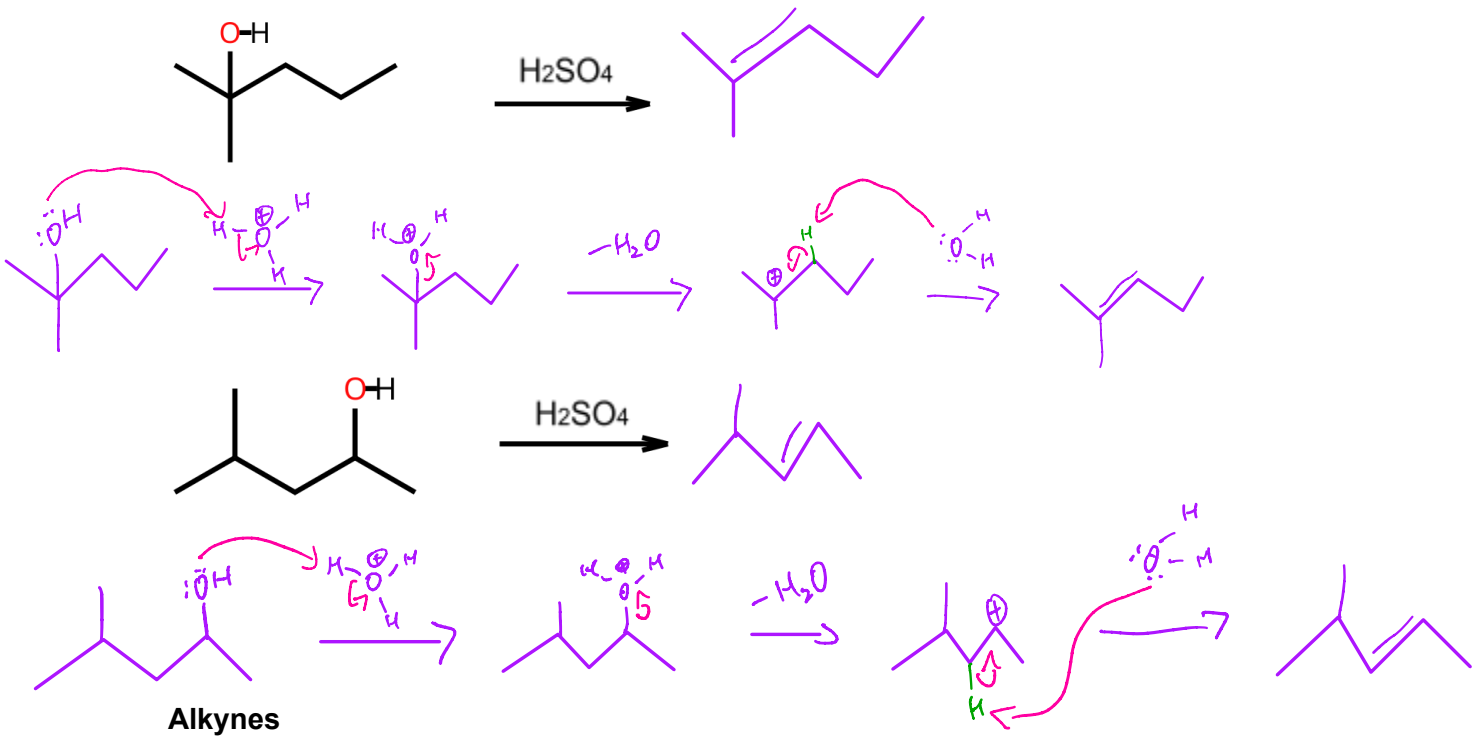



(2Z)-2-bromo-5-methyl-2-hexene



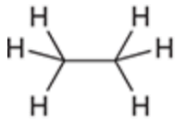
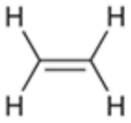
(3E)-3-methyl-3-hexene

**Predict the dehydration products below:**



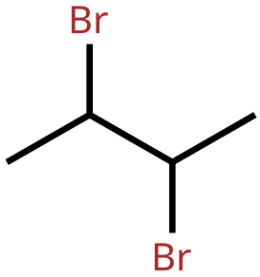
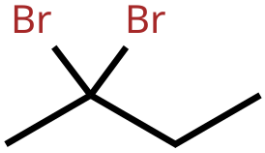

**Alkynes**

**Acidity of alkynes**

| Ethane | Ethylene | Acetylene |
|---|---|---|
|  |  |  |
| $pK_a = 50$ | $pK_a = 44$ | $pK_a = 25$ |

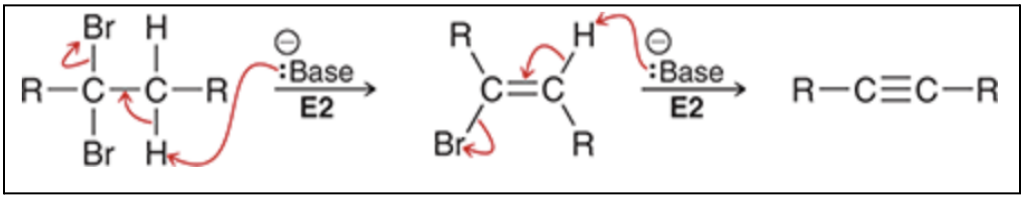
**Synthesizing alkynes via dehydrohalogenation**

"Jammed"

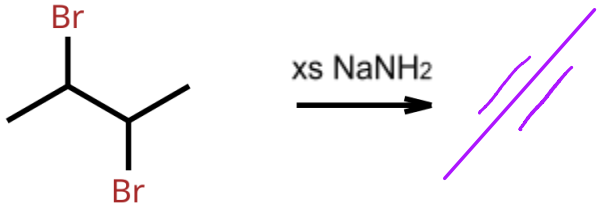
| Vicinal Dihalide | Geminal Dihalide |
|---|---|
|  |  |

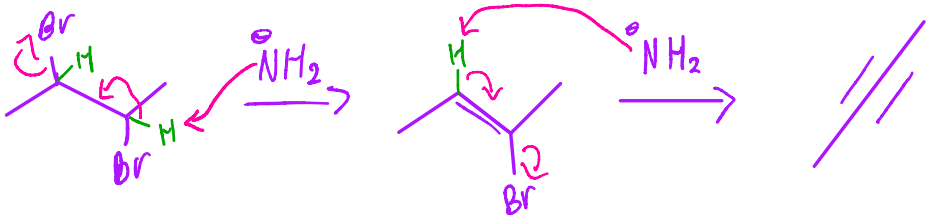
2 E2 mech

Mechanism:

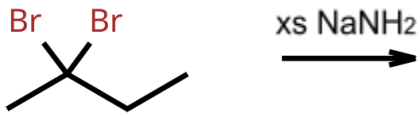


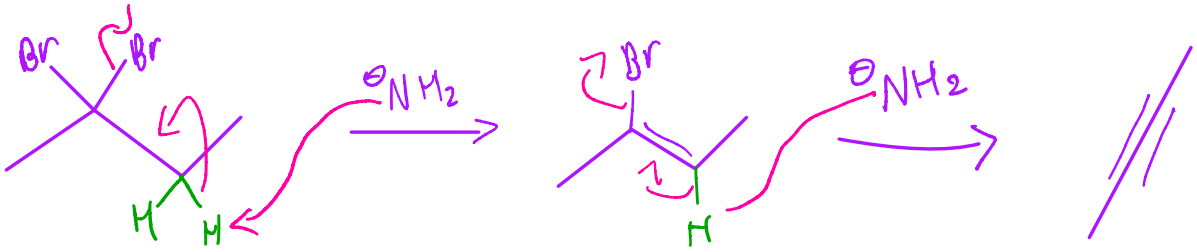

Vicinal Dihalide:



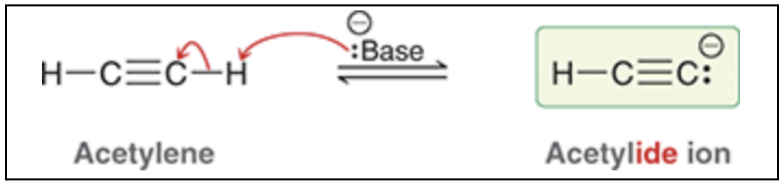




Geminal Dihalide:

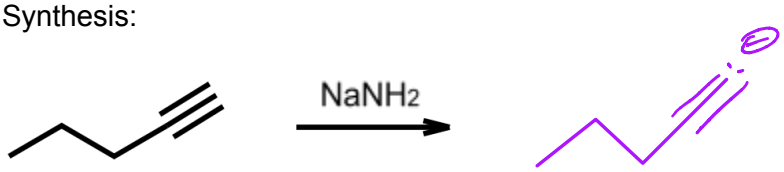


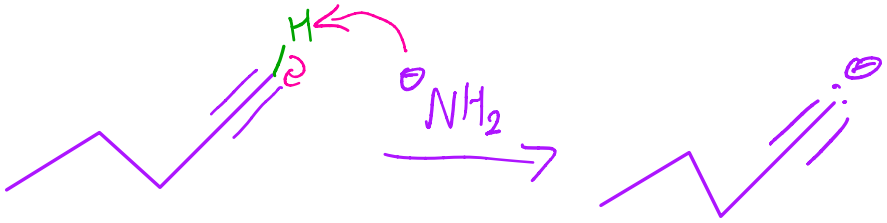



Acetylide Anion:

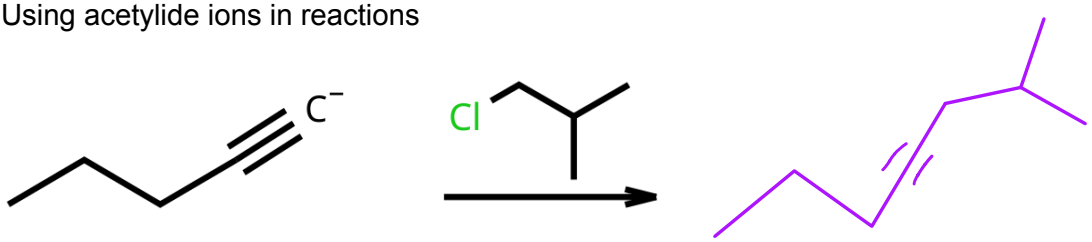


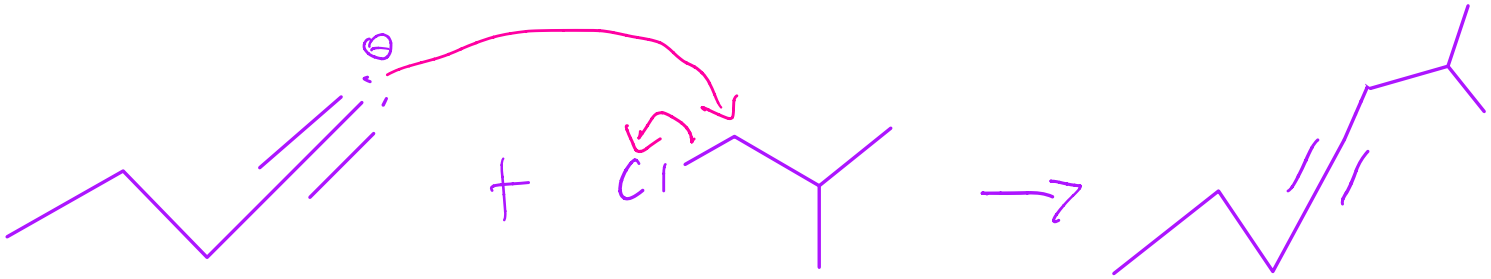

Synthesis:



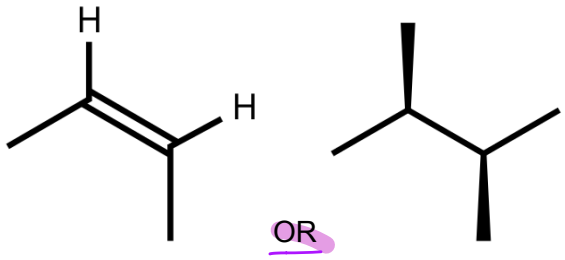
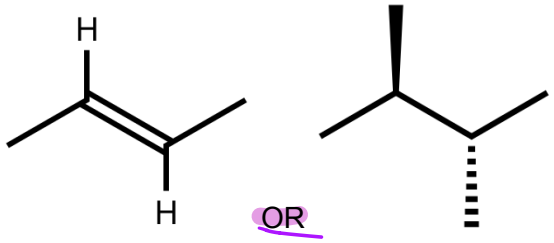




Using acetylide ions in reactions



**Syn and Anti-Addition**

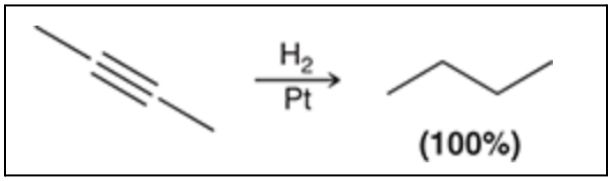
| Syn-Addition | Anti-Addition |
|---|---|
| 2 groups added to the same face of a π bond | 2 groups are added to opposite faces of the π bond |
|   |   |

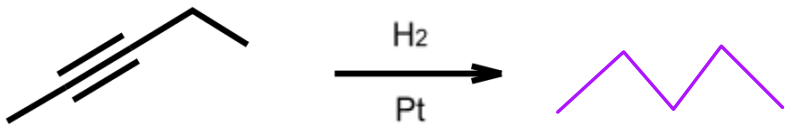
**Reduction via catalytic hydrogenation**

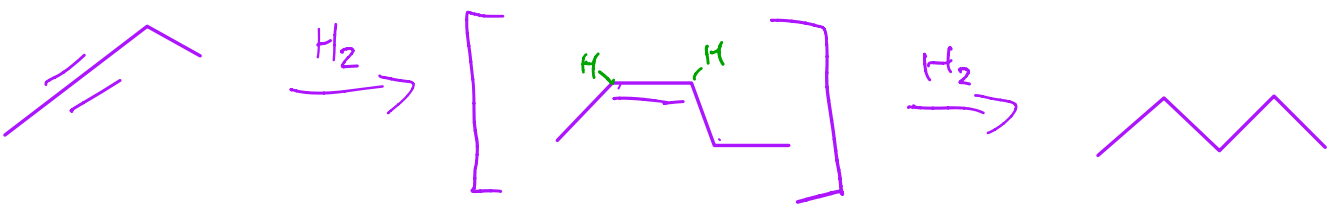
Similar to converting an alkene to an alkane, we can convert an alkyne to an alkane

Via hydrogenation

Uses syn addition



**Using a poisoned catalyst**

Under regular hydrogenation, it is difficult to isolate the cis-alkene intermediate. To stop the reaction at a cis-alkene we use a Poisoned catalyst (aka Lindlar's Catalyst or P-2)


Lindlar's Catalyst:

- most common
- Pd/CaCO3, quinoline

P-2 Catalyst:

- Nickel boride
- Ni2B (P-2)

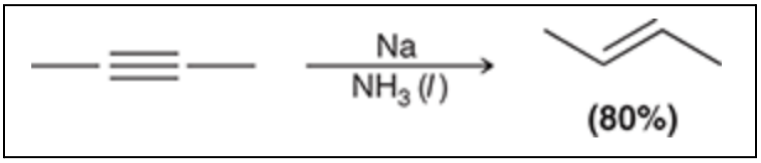


Syn-addition

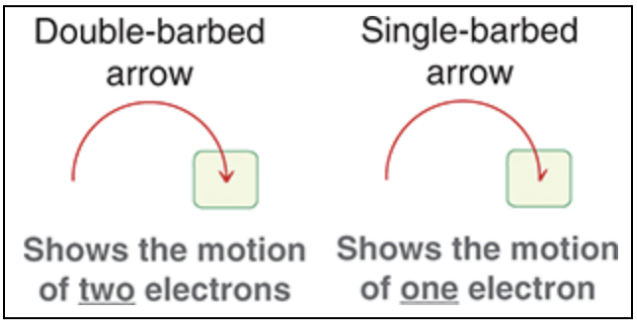
**Dissolving Metal Reduction**

Alkyne to trans Alkene via an anti addition

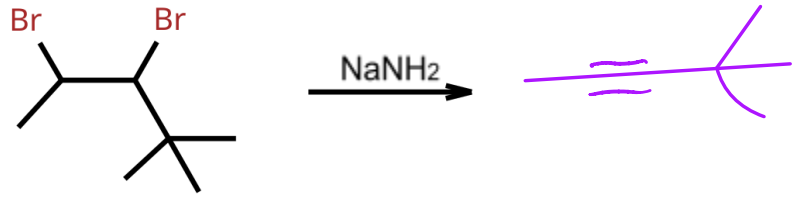
* uses radicals *

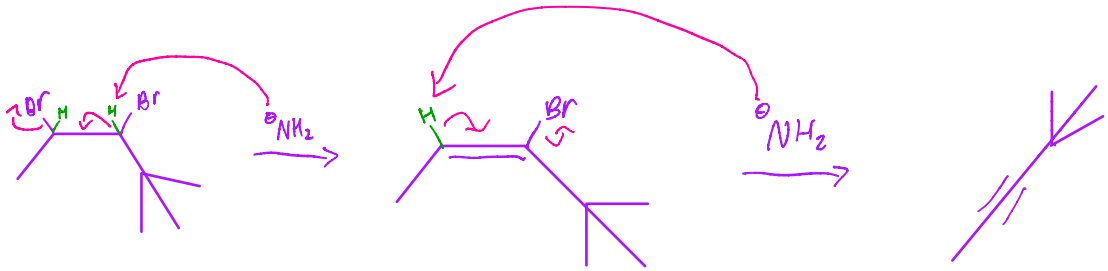


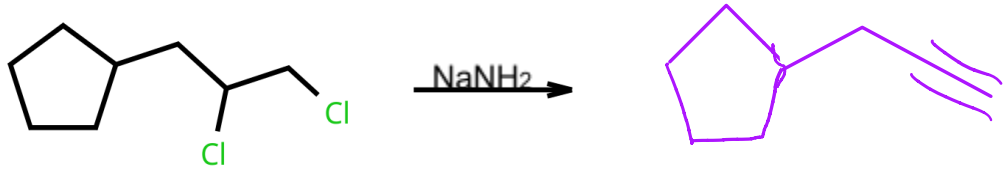

PSA: Pay attention to the arrows being used!

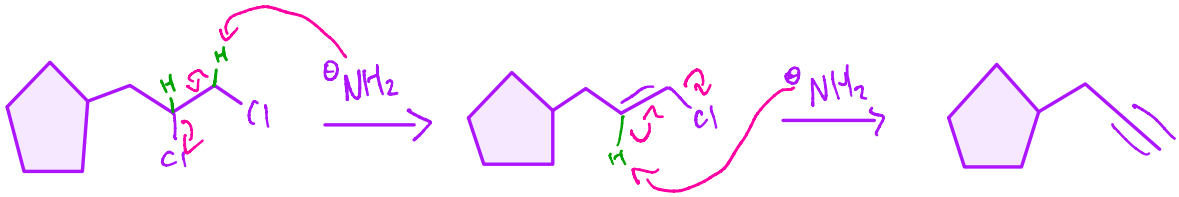


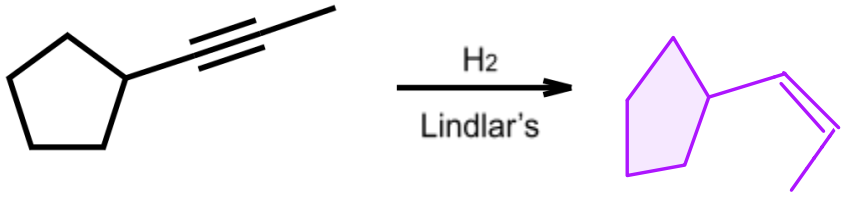

**Practice**

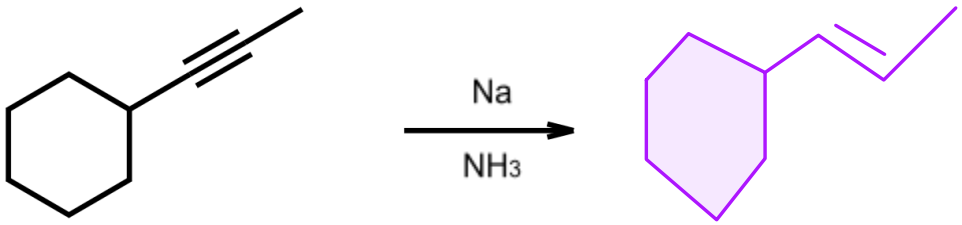


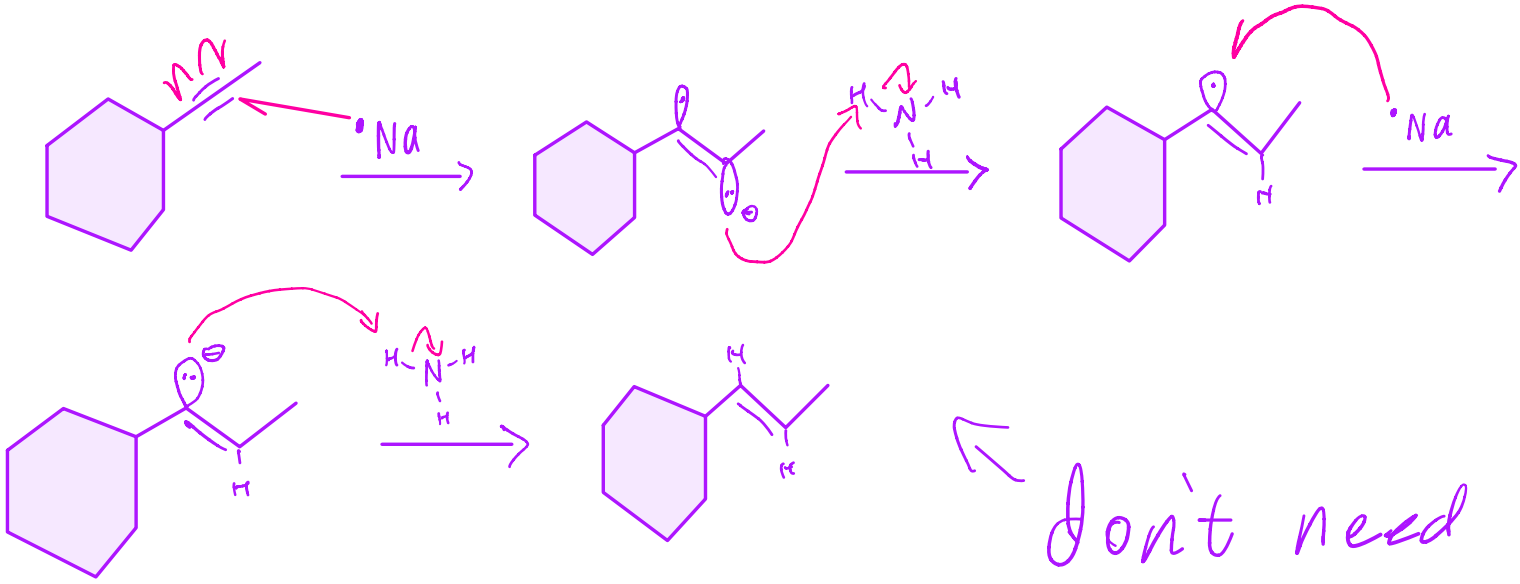






don't need this mech, just an example :)